



VPI92-07CIP2ADIV3CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT APPLICATION

Applicants : Roger D. Tung, et al.

Application No.: 10/786,997 Confirmation No.: 9030

Filed : February 24, 2004

FOR : NOVEL SULFONAMIDE INHIBITORS OF

ASPARTYL PROTEASE

Examiner : D. Margaret Seaman

Group Art Unit : 1625

New York, New York 10020 January 7, 2005

Hon. Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Sir:

Pursuant to 37 C.F.R. §§ 1.56 and 1.97(c), applicants, through their attorneys, hereby make the following patents and publications of record in the above-identified patent application*:

UNITED STATES PATENTS

Mohrs et al.	3,743,722	07/03/1973
Descamps et al.	4,330,542	05/18/1982
Ryono et al.	4,629,724	12/16/1986

^{*} For the convenience of the Examiner, a completed Form PTO/SB/08A(10-01), listing these documents, is attached.

Martin et al.

5,196,438

03/23/1993

Kempf et al.

5,354,866

10/11/1994

FOREIGN PATENT DOCUMENTS

EP-0 022 118	01/07/1981	Sanofi SA
EP-0 181 071	03/14/1986	Squibb & Sons, Inc.
EP-0 264 795	04/27/1988	Merck Patent GmbH
EP-0 346 847	12/20/1989	Hoffmann LaRoche
EP-0 364 804	04/ 25/1990	Abbott Laboratories
EP-0 468 641	01/29/1992	Shionogi & Co.
EP-0 486 948	05/27/1992	Abbott Laboratories
EP-0 541 168	05/12/1993	Merck & Co. Inc.
DE-3542567	06/05/1986	Squibb & Sons, Inc.
GB-2,167,759	6/04/1986	Squibb & Sons, Inc.
GB-2,200,115	07/27/1988	Sandoz Ltd.
JP-59046252	03/15/1984	Dainippon Ink & Chemicals; Dainippon Ink Rikagaku Kenkuys
JP-59048449	03/19/1984	Dainippon Ink & Chemicals; Dainippon Ink Rikagaku Kenkuys
JP-61071830	04/12/1986	Dainippon Ink & Chemicals
WO-90/07329	07/12/1990	University of California
WO-91/00725	01/24/1991	Abbott Laboratories
WO-91/18866	12/12/1991	Du Pont Merck Pharma
WO-92/08688	05/29/1992	Monsanto Co.
WO-92/08698	05/29/1992	Monsanto Co.
WO-92/08699	05/29/1992	Monsanto Co.
WO-92/08700	05/29/1992	Monsanto Co.
WO-92/08701	05/29/1992	Monsanto Co.; Searle & Co.
WO-92/17176	10/15/1992	Abbott Laboratories
WO-93/23368	11/25/1993	Searle & Co.; Monsanto Co.
WO-93/23388	11/25/1993	Searle & Co.; Monsanto Co.
WO-93/23379	11/25/1993	Monsanto Co.

WO-94/04491	03/3/1994	Searle & Co.; Monsanto Co.
WO-94/04492	03/03/1994	Searle & Co.; Monsanto Co.
WO-94/04493	03/03/1994	Searle & Co.; Monsanto Co.
WO-94/10134	05/11/1994	Searle & Co.; Monsanto Co.
WO-94/10136	05/11/1994	Searle & Co.; Monsanto Co.
WO-94/18192	08/18/1994	Merck & Co. Inc.
WO-94/19322	09/01/1994	Chugai Pharmaceuticals Ltd.; Esaki Toru

OTHER PUBLICATIONS

- R.D. Bindal et al., "Ab Initio Calculations on N-Methylmethanesulfonamide and Methyl Methanesulfonate for the Development of Force Field Torsional Parameters and Their Use in the Conformational Analysis of Some Novel Estrogens", J. Am. Chem. Soc., 112, pp. 7861-68 (1990).
- R. Bone et al., "X-ray Crystal Structure of the HIV Protease Complex with L-700,417, an Inhibitor with Pseudo C_2 Symmetry", J. Am. Chem. Soc., 113, pp. 9382-84 (1991).
- R.F. Borch et al., "The Cyanohydridoborate Anion as a Selective Reducing Agent", J. Am. Chem. Soc., 93, pp. 2897-904 (1971).
- J.C. Craig et al., "Antiviral Synergy Between Inhibitors of HIV Proteinase and Reverse Transcriptase", Antiviral Chem. and Chemotherapy, 4(3), pp. 161-66 (1990).
- S. Crawford et al., "A Deletion Mutation in the 5' Part of the pol Gene of Moloney Murine Leukemia Virus Blocks Proteolytic Processing of the gag and pol Polyproteins", J. Virol., 53, pp. 899-907 (1985).
- M. Cushman et al., "Delvelopment of Methodology for the Synthesis of Stereochemically Pure Pheψ [CH2N]Pro Linkages in HIV Protease Inhibitors", J. Org. Chem., 56, pp. 4161-67 (1991).
- D.S. Dhanoa et al., "The Synthesis of Potent Macrocyclic Renin Inhibitors", Tetrahedron Lett., 33, pp. 1725-28 (1992).
- G.B. Dreyer et al., "Hydroxyethylene Isostere Inhibitors of Human Immunodeficiency Virus-1 Protease:

- Structure-Activity Analysis Using Enzyme Kinetics, X-ray Crystallography, and Infected T-Cell Assays", Biochemistry, 31, pp. 6646-59 (1992).
- B.E. Evans et al., "A Stereocontrolled Synthesis of Hydroxyethylene Dipeptide Isosteres Using Novel, Chiral Aminoalkyl Epoxides and γ -(Aminoalkyl) γ -Lactones", J. Org. Chem., 50, pp. 4615-25 (1985).
- G.A. Flynn et al., "An Acyl-Iminium Ion Cyclization Route to a Novel Conformationally Restricted Dipeptide Mimic: Applications to Angiotensin-Converting Enzyme Inhibition", J. Am. Chem. Soc., 109, pp, 7914-15 (1989).
- G. Fontenot et al., "PCR Amplification of HIV-1 Proteinase Sequences Directly from Lab Isolates Allows Determination of Five Conserved Domains", Virology, 190, pp. 1-10 (1992).
- P.G. Gassman and T.L. Guggenheim, "Opening of Epoxides with Trimethylsilyl Cyanide to Produce β -Amino Alcohols", J. Am. Chem. Soc., 104, pp. 5849-50 (1982).
- E.E. Gilbert, "Recent Developments in Preparative Sulfonation and Sulfation", Synthesis, 1969, pp. 3-10 (1969).
- A. Goldblum, "Modulation of the Affinity of Aspartic Proteases by the Mutated Residues in Active Site Models", FEBS, 261, pp. 241-44 (1990).
- D. Grobelny et al., "Selective Phosphinate Transition-State Analogue Inhibitors of the Protease of Human Immunodeficiency Virus", Biochem. Biophys. Res. Commun., 169, pp. 1111-16 (1990).
- G.D. Hartman et al., "4-Substituted Thiophene- and Furan-2-sulfonamides as Topical Carbonic Anhydrase Inhibitors", J. Med. Chem., 35, pp. 3822-31 (1992).
- J.R. Huff, "HIV Protease: A Novel Chemotherapeutic Target for AIDS", Journal of Medicinal Chemistry, 34(8), pp. 2305-14 (1991).
- K.Y. Hui et al., "A Rational Approach in the Search for Potent Inhibitors Against HIV Proteinase", FASEB, 5, pp. 2606-10 (1991).

- N.E. Kohl et al., "Active HIV Protease Is Required for Viral Infectivity", Proc. Natl. Acad. Sci. USA, 85, pp. 4686-90 (1988).
- X. Lin et al., "Enzymic Activities of Two-Chain Pepsinogen, Two-Chain Pepsin, and the Amino-Terminal Lobe of Pepsinogen", J. Biol. Chem., 267(24), pp. 17257-63 (1992).
- K.P. Manfredi et al., "Examination of HIV-1 Protease Secondary Structure Specificity Using Conformationally Constrained Inhibitors", J. Med. Chem., 34, pp. 3395-99 (1991).
- F.R. Marshall, "Computer-Aided Drug Design", Ann. Ref. Pharmacol. Toxicol., 27. pp. 193-213 (1987).
- J.A. Martin, "Recent Advances in the Design of HIV Proteinase Inhibitors", Antiviral Research, 17, pp. 265-78 (1992).
- T.D. Meek et al., "Inhibition of HIV-1 Protease in Infected T-Lymphocytes by Synthetic Peptide Analogues", Nature, 343, pp. 90-92 (1990).
- M. Miller et al., "Structure of Complex of Synthetic HIV-1 Protease with a Substrate-Based Inhibitor at 2.3 Å Resolution", Science, 246, pp. 1149-52 (1989).
- M. Miller et al., "Crystal Structure of a Retroviral Protease Proves Relationship to Aspartic Protease Family", Nature, 337, pp. 576-79 (1989).
- H. Mitsuya and S. Broder, "Inhibition of the in vitro Infectivity and Cytopathic Effect of Human T-Lymphotropic Virus Type III/Lymphoadenopathy-Associated Virus (HTLV-III/LAV) by 2',3'-Dideoxynucleosides", Proc. Natl. Acad. Sci. USA, 83, pp. 1911-15 (1986).
- K.H.M. Murthy et al., "Crystal Structures at 2.2-Å Resolution of Hydroxyethylene-Based Inhibitors Bound to Human Immunodeficiency Virus Type 1 Protease Show That the Inhibitors Are Present in Two Distinct Orientations", J. Biol. Chem., 267, pp.22770-78 (1992).
- J.B. Nichols et al., "A Molecular Mechanics Valence Force Field for Sulfonamides Derived by ab initio Methods", J. Phys. Chem., 95, pp. 9803-11 (1991).

- L.E. Overman and L.A. Flippin, "Facile Aminolysis of Epoxides with Diethylaluminum Amides", Tetrahedron Letters, 195, pp. 195-98 (1981).
- J. Palca, "Shooting at a New HIV Target", Science, 247, p. 410 (1990).
- L.H. Pearl et al., "A Structural Model for the Retroviral Proteases", Nature, 329. pp. 329-51 (1987).
- M. Popvic et al., "Detection, Isolation, and Continuous Production of Cytopathic Retroviruses (HTLV-III) from Patients with AIDS and Pre-AIDS", Science, 224, pp. 497-500 (1984).
- G.H. Posner and D.Z. Rogers, "Organic Reactions at Alumina Surfaces. Mild and Selective Opening of Epoxides by Alcohols, Thiols, Benzeneselenol, Amines, and Acetic Acid", J. Am. Chem. Soc., 99, 8208-18 (1977).
- M.D. Power et al., "Nucleotide Sequence of SRV-1, a Type D Simian Acquired Immune Deficiency Syndrome Retrovirus" Science, 231, pp. 1567-73 (1986).
- N.A. Roberts, "Rational Design of Peptide-Based HIV Proteinase Inhibitors", Science, 248, pp. 358-61 (1990).
- S. Scharpe et al., "Proteases and Their Inhibitors: Today and Tomorrow", Biochimie, 73, pp. 121-26 (1991).
- S.K. Sharma et al., "Could Angiotensin I Be Produced from a Renin Substrate by the HIV-1 Protease?", Anal. Biochem., 198, pp. 363-67 (1991).
- H. Toh et al., "Close Structural Resemblance Between Putative Polymerase of a Drosophila Transposable Genetic Element 17.6 and pol Gene Product of Moloney Murine Leukemia Virus", EMBO J., 4. pp. 1267-72 (1985).

Each of the above listed documents was submitted with applicants' November 24, 1993 Information Disclosure Statement in U.S. application No. 08/142,327, now U.S. Patent 5,583,397, from which the present application claims priority. Therefore, no copy of the documents are provided herewith. 37 C.F.R. § 1.98(d). However, if the Examiner

desires applicants to resubmit these documents, applicants request that the Examiner notify applicants in the next communication.

This Statement is submitted after the mailing date of the first Office Action. In accordance with 37 C.F.R. § 1.97, this Statement is accompanied by the fee as set forth in 37 C.F.R. § 1.17(p). If for any reason any additional fee is due, the Director is hereby authorized to charge payment of any fees required in connection with this Information Disclosure Statement to Deposit Account No. 06-1075. A duplicate copy of this letter is transmitted herewith.

Applicants respectfully request that these documents be (1) considered by the Examiner prior to issuance of any patent from this application; and (2) printed on any patent that may issue from this application. Applicants also request that a copy of enclosed Form PTO/SB/08A(10-01), as considered and initialed by the Examiner, be returned with the next communication.

Respectfully submitted,

I hereby certify that this
Correspondence is being
deposited with the U.S.
Postal Service as First
Class Mail in an envelope
Addressed to:
Commissioner for Patents
P.O. Box 1450

January 7,2005

Alexandria, VA 22313-1450 on

dyature of Person Signing

James F. Haley, Jr. (Reg. No. 27,794) Karen Mangasarian (Reg. No. 43,772)

Attorneys for Applicants

Fish & Neave IP Group
Ropes & Gray LLP
Customer No. 1473
1251 Avenue of the Americas
New York, New York 10020-1104
Tel.: (212) 596-9000

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE der the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Complete if known Substitute for form 1449A/PTO **Application Number** 10/786.997 INFORMATION DISCLOSURE **Filing Date** February 24, 2004 **First Named Inventor** STATEMENT BY APPLICANT Roger D. Tung et al. Art Unit 1625 (use as many sheets as necessary) **Examiner Name** D. Margaret Seaman Sheet Attorney Docket Number VPI/92-07CIP2ADIV3 CON

			U.S. PATENT I	OCUMENTS	
Examiner Cite	Cite	Document Number	Publication Date	Name of Patentee or	Pages, Columns, Lines, Where
initials*	No.1	Number – Kind Code ^z (if known)	MM-DD-YYYY	Applicant of Cited Documents	Relevant Passages or Relevant Figures Appear
•		US- 3,743,722	07/03/1973	Mohrs et al.	
		US- 4,330,542	05/18/1982	Descamps et al.	
_		US- 4,629,724	12/16/1986	Ryono et al.	
		US- 5,196,438	03/23/1993	Martin et al.	
		US- 5,354,866	10/11/1994	Kempf et al.	
			<u> </u>		
					4

		FO	REIGN PATENT	T DOCUMENTS	•	
Examiner initials*	Cite No.1	Foreign Patent Document Country Code ³ - Number ⁴ - Kind Code ⁵ (<i>if known</i>)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T°
		EP-0 022 118	01/07/1981	Sanofi SA		
		EP-0 181 071	03/14/1986	Squibb & Sons, Inc.		
		EP-0 264 795	04/27/1988	Merck Patent GmbH		
·		EP-0 346 847	12/20/1989	Hoffmann LaRoche		
		EP-0 364 804	04/ 25/1990	Abbott Laboratories		
		EP-0 468 641	01/29/1992	Shionogi & Co.		<u> </u>
		EP-0 486 948	05/27/1992	Abbott Laboratories		
	•	EP-0 541 168	05/12/1993	Merck & Co. Inc.		7
		DE-3542567	06/05/1986	Squibb & Sons, Inc.		<u> </u>
		GB-2,167,759	6/04/1986	Squibb & Sons, Inc.		
		GB-2,200,115	07/27/1988	Sandoz Ltd.		
		JP-59046252	03/15/1984	Dainippon Ink & Chemicals; Dainippon Ink Rikagaku Kenkuys		_
		JP-59048449	03/19/1984	Dainippon Ink & Chemicals; Dainippon Ink Rikagaku Kenkuys		,

Examiner Signature	Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.usplo.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

Approved for use through 10/31/2002. OMB 0651-0031 U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control in

Substitute for form 1449A/PTO			то	Con	plete if known	
		Application Number	10/786,997			
INFORMATION DISCLOSURE		Filing Date	February 24, 2004			
STA	STATEMENT BY APPLICANT		First Named Inventor	Roger D. Tung et al.		
					Art Unit	1625
(use	as ma	ny shee	ts as	necessary)	Examiner Name	D. Margaret Seaman
Sheet	2		of	5	Attorney Docket Number	VPI/92-07CIP2ADIV3 CON

		FO	REIGN PATENT	F DOCUMENTS		
Examiner initials*	Cite No.1	Foreign Patent Document Country Code ³ - Number ⁴ - Kind Code ⁵ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	. T ⁰
		JP-61071830	04/12/1986	Dainippon Ink & Chemicals		
		WO-90/07329	07/12/1990	University of California		
		WO-91/00725	01/24/1991	Abbott Laboratories		-
		WO-91/18866	12/12/1991	Du Pont Merck Pharma		
		WO-92/08688	05/29/1992	Monsanto Co.		
		WO-92/08698	05/29/1992	Monsanto Co.		
		WO-92/08699	05/29/1992	Monsanto Co.		٠.
		WO-92/08700	05/29/1992	Monsanto Co.		
		WO-92/08701	05/29/1992	Monsanto Co.; Searle & Co.		
		WO-92/17176	10/15/1992	Abbott Laboratories		
		WO-93/23368	11/25/1993	Searle & Co.; Monsanto Co.		
		WO-93/23388	11/25/1993	Searle & Co.; Monsanto Co.		
		WO-93/23379	11/25/1993	Monsanto Co.		
		WO-94/04491	03/3/1994	Searle & Co.; Monsanto Co.		
		WO-94/04492	03/03/1994	Searle & Co.; Monsanto Co.		
	(.	WO-94/04493	03/03/1994	Searle & Co.; Monsanto Co.		
		WO-94/10134	05/11/1994	Searle & Co.; Monsanto Co.		
		WO-94/10136	05/11/1994	Searle & Co.; Monsanto Co.		
		WO-94/18192	08/18/1994	Merck & Co. Inc.		
-		WO-94/19322	09/01/1994	Chugai Pharmaceuticals Ltd.; Esaki Toru		
						·
					4	-
		 				-

Examiner	 Date	
Signature	Considered	

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. "EXAMINER: Initial if reference considered, whether or not clauon is in conformance with MPEP out. Draw line unduly is full in conformance and not considered, include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection

Substitute for form 1449A/PTO				Con	nplete if known
				Application Number	10/786,997
INFORMATION DISCLOSURE				Filing Date	February 24, 2004
STA	STATEMENT BY APPLICANT		First Named Inventor	Roger D. Tung et al.	
		:		Art Unit	1625
(use	(use as many sheets as necessary)		Examiner Name	D. Margaret Seaman	
Sheet	3	of	5	Attorney Docket Number	VPI/92-07CIP2ADIV3 CON

	Γ	NON PATENT LITERATURE DOCUMENTS	
Examiner initials*	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	Τ²
		R.D. Bindal et al., "Ab Initio Calculations on N-Methylmethanesulfonamide and Methyl Methanesulfonate for the Development of Force Field Torsional Parameters and Their Use in the Conformational Analysis of Some Novel Estrogens", <u>J. Am. Chem. Soc.</u> , 112, pp. 7861-68 (1990).	
		R. Bone et al., "X-ray Crystal Structure of the HIV Protease Complex with L-700,417, an Inhibitor with Pseudo C ₂ Symmetry", <u>J. Am. Chem. Soc.</u> , 113, pp. 9382-84 (1991).	
		R.F. Borch et al., "The Cyanohydridoborate Anion as a Selective Reducing Agent", <u>J. Am.</u> Chem. Soc., 93, pp. 2897-904 (1971).	
	<u> </u>	J.C. Craig et al., "Antiviral Synergy Between Inhibitors of HIV Proteinase and Reverse Transcriptase", Antiviral Chem. and Chemotherapy, 4(3), pp. 161-66 (1990).	
	- (-	S. Crawford et al., "A Deletion Mutation in the 5' Part of the pol Gene of Moloney Murine Leukemia Virus Blocks Proteolytic Processing of the gag and pol Polyproteins", <u>J. Virol.</u> , 53, pp. 899-907 (1985).	
-		M. Cushman et al., "Delvelopment of Methodology for the Synthesis of Stereochemically Pure Pheψ[CH₂N]Pro Linkages in HIV Protease Inhibitors", <u>J. Org. Chem.</u> , 56, pp. 4161-67 (1991).	
		D.S. Dhanoa et al., "The Synthesis of Potent Macrocyclic Renin Inhibitors", <u>Tetrahedron</u> Lett., 33, pp. 1725-28 (1992).	
		G.B. Dreyer et al., "Hydroxyethylene Isostere Inhibitors of Human Immunodeficiency Virus- 1 Protease: Structure-Activity Analysis Using Enzyme Kinetics, X-ray Crystallography, and Infected T-Cell Assays", <u>Biochemistry</u> , 31, pp. 6646-59 (1992).	
		B.E. Evans et al., "A Stereocontrolled Synthesis of Hydroxyethylene Dipeptide Isosteres Using Novel, Chiral Aminoalkyl Epoxides and γ-(Aminoalkyl) γ-Lactones", <u>J. Org. Chem.</u> , 50, pp. 4615-25 (1985).	
		G.A. Flynn et al., "An Acyl-Iminium Ion Cyclization Route to a Novel Conformationally Restricted Dipeptide Mimic: Applications to Angiotensin-Converting Enzyme Inhibition", J. Am. Chem. Soc., 109, pp, 7914-15 (1989).	,
		G. Fontenot et al., "PCR Amplification of HIV-1 Proteinase Sequences Directly from Lab Isolates Allows Determination of Five Conserved Domains", <u>Virology</u> , 190, pp. 1-10 (1992).	
		P.G. Gassman and T.L. Guggenheim, "Opening of Epoxides with Trimethylsilyl Cyanide to Produce β-Amino Alcohols", J. Am. Chem. Soc., 104, pp. 5849-50 (1982).	
		E.E. Gilbert, "Recent Developments in Preparative Sulfonation and Sulfation", <u>Synthesis</u> , 1969, pp. 3-10 (1969).	
		A. Goldblum, "Modulation of the Affinity of Aspartic Proteases by the Mutated Residues in Active Site Models", FEBS, 261, pp. 241-44 (1990).	
		D. Grobelny et al., "Selective Phosphinate Transition-State Analogue Inhibitors of the Protease of Human Immunodeficiency Virus", <u>Biochem. Biophys. Res. Commun.</u> , 169, pp. 1111-16 (1990).	

Fuendana		
Examiner Signature	Date	
Orginatare	Considered	

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English tanguage Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentially is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Tradermark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE Under the Paperwork Reduction Act of 1995, no persons are required

Substitu	ute for	form 1	449A/F	TO	Complete if known		
					Application Number	10/786,997	
				CLOSURE	Filing Date	February 24, 2004	
STA	STATEMENT BY APPLICANT			PLICANT	First Named Inventor	Roger D. Tung et al.	
					Art Unit	1625	
(use	as m	any sh	eets as	necessary)	Examiner Name	D. Margaret Seaman	
Sheet	4	w.	of	5	Attorney Docket Number	VPI/92-07CIP2ADIV3 CON	

		NON PATENT LITERATURE DOCUMENTS		
Examiner initials*	No. item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number publisher, city and/or country where published			
	_	G.D. Hartman et al., "4-Substituted Thiophene- and Furan-2-sulfonamides as Topical Carbonic Anhydrase Inhibitors", J. Med. Chem., 35, pp. 3822-31 (1992).		
		J.R. Huff, "HIV Protease: A Novel Chemotherapeutic Target for AIDS", <u>Journal of Medicinal Chemistry</u> , 34(8), pp. 2305-14 (1991).		
		K.Y. Hui et al., "A Rational Approach in the Search for Potent Inhibitors Against HIV Proteinase", FASEB, 5, pp. 2606-10 (1991).	7	
	<u>.</u>	N.E. Kohl et al., "Active HIV Protease Is Required for Viral Infectivity", Proc. Natl. Acad. Sci. USA, 85, pp. 4686-90 (1988).		
	· .	X. Lin et al., "Enzymic Activities of Two-Chain Pepsinogen, Two-Chain Pepsin, and the Amino-Terminal Lobe of Pepsinogen", <u>J. Biol. Chem.</u> , 267(24), pp. 17257-63 (1992).		
		K.P. Manfredi et al., "Examination of HIV-1 Protease Secondary Structure Specificity Using Conformationally Constrained Inhibitors", <u>J. Med. Chem.</u> , 34, pp. 3395-99 (1991).		
,,		F.R. Marshall, "Computer-Aided Drug Design", Ann. Ref. Pharmacol. Toxicol., 27. pp. 193-213 (1987).		
	·	J.A. Martin, "Recent Advances in the Design of HIV Proteinase Inhibitors", Antiviral Research, 17, pp. 265-78 (1992).		
		T.D. Meek et al., "Inhibition of HIV-1 Protease in Infected T-Lymphocytes by Synthetic Peptide Analogues", Nature, 343, pp. 90-92 (1990).		
		M. Miller et al., "Structure of Complex of Synthetic HIV-1 Protease with a Substrate-Based Inhibitor at 2.3 Å Resolution", Science, 246, pp. 1149-52 (1989).	3 ·	
		M. Miller et al., "Crystal Structure of a Retroviral Protease Proves Relationship to Aspartic Protease Family", Nature, 337, pp. 576-79 (1989).		
		H. Mitsuya and S. Broder, "Inhibition of the in vitro Infectivity and Cytopathic Effect of Human T-Lymphotropic Virus Type III/Lymphoadenopathy-Associated Virus (HTLV-III/LAV) by 2',3'-Dideoxynucleosides", Proc. Natl. Acad. Sci. USA, 83, pp. 1911-15 (1986).	<u> </u>	
		K.H.M. Murthy et al., "Crystal Structures at 2.2-Å Resolution of Hydroxyethylene-Based Inhibitors Bound to Human Immunodeficiency Virus Type 1 Protease Show That the Inhibitors Are Present in Two Distinct Orientations", J. Biol. Chem., 267, pp.22770-78 (1992).		
		J.B. Nichols et al., "A Molecular Mechanics Valence Force Field for Sulfonamides Derived by ab initio Methods", J. Phys. Chem., 95, pp. 9803-11 (1991).		
		L.E. Overman and L.A. Flippin, "Facile Aminolysis of Epoxides with Diethylaluminum Amides", <u>Tetrahedron Letters</u> , 195, pp. 195-98 (1981).		
Œ		J. Palca, "Shooting at a New HIV Target", Science, 247, p. 410 (1990).		
	l	L.H. Pearl et al., "A Structural Model for the Retroviral Proteases", Nature, 329. pp. 329-51 (1987).		

Examiner	Date	
Signature	Considered	·

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
pond to a collection of information unless it contains a valid OMB control number. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it

Substitu	ute for form 144	49A/P	то	Complete if known		
				Application Number	10/786,997	
INFO	DRMATION	DISC	CLOSURE	Filing Date	February 24, 2004	
STA	STATEMENT BY APPLICANT			First Named Inventor	Roger D. Tung et al.	
				Art Unit	1625	
(use	as many shee	ets as	necessary)	Examiner Name	D. Margaret Seaman	
Sheet	5	of	5	Attorney Docket Number	VPI/92-07CIP2ADIV3 CON	

		NON PATENT LITERATURE DOCUMENTS	
Examiner initials*	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T²
		M. Popvic et al., "Detection, Isolation, and Continuous Production of Cytopathic Retroviruses (HTLV-III) from Patients with AIDS and Pre-AIDS", <u>Science</u> , 224, pp. 497-500 (1984).	
		G.H. Posner and D.Z. Rogers, "Organic Reactions at Alumina Surfaces. Mild and Selective Opening of Epoxides by Alcohols, Thiols, Benzeneselenol, Amines, and Acetic Acid", J. Am. Chem. Soc., 99, 8208-18 (1977).	
		M.D. Power et al., "Nucleotide Sequence of SRV-1, a Type D Simian Acquired Immune Deficiency Syndrome Retrovirus" Science, 231, pp. 1567-73 (1986).	
		N.A. Roberts, "Rational Design of Peptide-Based HIV Proteinase Inhibitors", <u>Science</u> , 248, pp. 358-61 (1990).	*
		S. Scharpe et al., "Proteases and Their Inhibitors: Today and Tomorrow", Biochimie, 73, pp. 121-26 (1991).	
		S.K. Sharma et al., "Could Angiotensin I Be Produced from a Renin Substrate by the HIV-1 Protease?", Anal. Biochem., 198, pp. 363-67 (1991).	
	8	H. Toh et al., "Close Structural Resemblance Between Putative Polymerase of a Drosophila Transposable Genetic Element 17.6 and pol Gene Product of Moloney Murine Leukemia Virus", EMBO J., 4. pp. 1267-72 (1985).	
	_		
		0.	

Date	
Considered	

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

nder the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitu	ite for form 144	19A/P	то	Complete if known		
				Application Number	10/786,997	
INFO	PRMATION	DISC	CLOSURE	Filing Date	February 24, 2004	
STA	(use as many sheets as necessary)			First Named Inventor	Roger D. Tung et al.	
• • • • • • • • • • • • • • • • • • •				Art Unit	1625	
(use				Examiner Name	D. Margaret Seaman	
Sheet			Attorney Docket Number	VPI/92-07CIP2ADIV3 CON		

		Danimont Niverban		Name of Patentee or	Pages, Columns, Lines, Where
Examiner initials*	Cite No. ¹	Document Number Number – Kind Code ² (if known)	Publication Date MM-DD-YYYY	Applicant of Cited Documents	Relevant Passages or Relevant Figures Appear
		US- 3,743,722	07/03/1973	Mohrs et al.	
		US- 4,330,542	05/18/1982	Descamps et al.	
		US- 4,629,724	12/16/1986	Ryono et al.	
		US- 5,196,438	03/23/1993	Martin et al.	
		US- 5,354,866	10/11/1994	Kempf et al.	

		FO	REIGN PATENT	DOCUMENTS		
Examiner initials*	Cite No.1	Foreign Patent Document Country Code ³ - Number ⁴ - Kind Code ⁵ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		EP-0 022 118	01/07/1981	Sanofi SA		
		EP-0 181 071	03/14/1986	Squibb & Sons, Inc.		
		EP-0 264 795	04/27/1988	Merck Patent GmbH		
		EP-0 346 847	12/20/1989	Hoffmann LaRoche		
		EP-0 364 804	04/ 25/1990	Abbott Laboratories		
		EP-0 468 641	01/29/1992	Shionogi & Co.		
		EP-0 486 948	05/27/1992	Abbott Laboratories		
		EP-0 541 168	05/12/1993	Merck & Co. Inc.		
		DE-3542567	06/05/1986	Squibb & Sons, Inc.		
		GB-2,167,759	6/04/1986	Squibb & Sons, Inc.		
		GB-2,200,115	07/27/1988	Sandoz Ltd.		
		JP-59046252	03/15/1984	Dainippon Ink & Chemicals; Dainippon Ink Rikagaku Kenkuys		
		JP-59048449	03/19/1984	Dainippon Ink & Chemicals; Dainippon Ink Rikagaku Kenkuys		

Examiner	Date	2.80
Signature	Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

Approved for use through 10/31/2002. OMB 0651-0031 U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitu	ute for form 144	49A/P	то	Complete if known		
				Application Number	10/786,997	
INFO	DRMATION	DISC	CLOSURE	Filing Date	February 24, 2004	
STA	STATEMENT BY APPLICANT			First Named Inventor	Roger D. Tung et al.	
•			. 2.07	Art Unit	1625	
(use	(use as many sheets as necessary)			Examiner Name	D. Margaret Seaman	
Sheet	<u></u>		Attorney Docket Number	VPI/92-07CIP2ADIV3 CON		

		FO	REIGN PATENT	DOCUMENTS		
Examiner initials*	Cite No. ¹	Foreign Patent Document Country Code ³ - Number ⁴ - Kind Code ⁵ (<i>if known</i>)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T [®]
		JP-61071830	04/12/1986	Dainippon Ink & Chemicals		
		WO-90/07329	07/12/1990	University of California		
		WO-91/00725	01/24/1991	Abbott Laboratories		
		WO-91/18866	12/12/1991	Du Pont Merck Pharma		
	!	WO-92/08688	05/29/1992	Monsanto Co.		
		WO-92/08698	05/29/1992	Monsanto Co.		
		WO-92/08699	05/29/1992	Monsanto Co.		
		WO-92/08700	05/29/1992	Monsanto Co.		-
		WO-92/08701	05/29/1992	Monsanto Co.; Searle & Co.		
		WO-92/17176	10/15/1992	Abbott Laboratories		
		WO-93/23368	11/25/1993	Searle & Co.; Monsanto Co.		
		WO-93/23388	11/25/1993	Searle & Co.; Monsanto Co.		
		WO-93/23379	11/25/1993	Monsanto Co.		
		WO-94/04491	03/3/1994	Searle & Co.; Monsanto Co.		
		WO-94/04492	03/03/1994	Searle & Co.; Monsanto Co.		
		WO-94/04493	03/03/1994	Searle & Co.; Monsanto Co.		
·		WO-94/10134	05/11/1994	Searle & Co.; Monsanto Co.		
-		WO-94/10136	05/11/1994	Searle & Co.; Monsanto Co.		
		WO-94/18192	08/18/1994	Merck & Co. Inc.		
		WO-94/19322	09/01/1994	Chugai Pharmaceuticals Ltd.; Esaki Toru		
						,

	The second secon	
Examiner	Date	
Signature	Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Complete if known Substitute for form 1449A/PTO **Application Number** 10/786,997 INFORMATION DISCLOSURE **Filing Date** February 24, 2004 **First Named Inventor** STATEMENT BY APPLICANT Roger D. Tung et al. Art Unit 1625 **Examiner Name** D. Margaret Seaman (use as many sheets as necessary) Sheet **Attorney Docket Number** VPI/92-07CIP2ADIV3 CON

		NON PATENT LITERATURE DOCUMENTS	
Examiner initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T²
		R.D. Bindal et al., "Ab Initio Calculations on N-Methylmethanesulfonamide and Methyl Methanesulfonate for the Development of Force Field Torsional Parameters and Their Use in the Conformational Analysis of Some Novel Estrogens", <u>J. Am. Chem. Soc.</u> , 112, pp. 7861-68 (1990).	
		R. Bone et al., "X-ray Crystal Structure of the HIV Protease Complex with L-700,417, an Inhibitor with Pseudo C ₂ Symmetry", <u>J. Am. Chem. Soc.</u> , 113, pp. 9382-84 (1991).	
		R.F. Borch et al., "The Cyanohydridoborate Anion as a Selective Reducing Agent", <u>J. Am. Chem. Soc.</u> , 93, pp. 2897-904 (1971).	
		J.C. Craig et al., "Antiviral Synergy Between Inhibitors of HIV Proteinase and Reverse Transcriptase", Antiviral Chem. and Chemotherapy, 4(3), pp. 161-66 (1990).	
		S. Crawford et al., "A Deletion Mutation in the 5' Part of the pol Gene of Moloney Murine Leukemia Virus Blocks Proteolytic Processing of the gag and pol Polyproteins", <u>J. Virol.,</u> 53, pp. 899-907 (1985).	
		M. Cushman et al., "Delvelopment of Methodology for the Synthesis of Stereochemically Pure Pheψ[CH ₂ N]Pro Linkages in HIV Protease Inhibitors", <u>J. Org. Chem.</u> , 56, pp. 4161-67 (1991).	
		D.S. Dhanoa et al., "The Synthesis of Potent Macrocyclic Renin Inhibitors", <u>Tetrahedron Lett.</u> , 33, pp. 1725-28 (1992).	
		G.B. Dreyer et al., "Hydroxyethylene Isostere Inhibitors of Human Immunodeficiency Virus-1 Protease: Structure-Activity Analysis Using Enzyme Kinetics, X-ray Crystallography, and Infected T-Cell Assays", Biochemistry, 31, pp. 6646-59 (1992).	
		B.E. Evans et al., "A Stereocontrolled Synthesis of Hydroxyethylene Dipeptide Isosteres Using Novel, Chiral Aminoalkyl Epoxides and γ -(Aminoalkyl) γ -Lactones", <u>J. Org. Chem.</u> , 50, pp. 4615-25 (1985).	-
		G.A. Flynn et al., "An Acyl-Iminium Ion Cyclization Route to a Novel Conformationally Restricted Dipeptide Mimic: Applications to Angiotensin-Converting Enzyme Inhibition", <u>J. Am. Chem. Soc.</u> , 109, pp, 7914-15 (1989).	
		G. Fontenot et al., "PCR Amplification of HIV-1 Proteinase Sequences Directly from Lab Isolates Allows Determination of Five Conserved Domains", Virology, 190, pp. 1-10 (1992).	
		P.G. Gassman and T.L. Guggenheim, "Opening of Epoxides with Trimethylsilyl Cyanide to Produce β-Amino Alcohols", J. Am. Chem. Soc., 104, pp. 5849-50 (1982).	
		E.E. Gilbert, "Recent Developments in Preparative Sulfonation and Sulfation", <u>Synthesis</u> , 1969, pp. 3-10 (1969).	
		A. Goldblum, "Modulation of the Affinity of Aspartic Proteases by the Mutated Residues in Active Site Models", <u>FEBS</u> , 261, pp. 241-44 (1990).	
		D. Grobelny et al., "Selective Phosphinate Transition-State Analogue Inhibitors of the Protease of Human Immunodeficiency Virus", <u>Biochem. Biophys. Res. Commun.</u> , 169, pp. 1111-16 (1990).	

Examiner	Date	
Signature	Considered	

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for réducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO			то	Complete if known	
				Application Number	10/786,997
INFORMATION DISCLOSURE STATEMENT BY APPLICANT			CLOSURE	Filing Date	February 24, 2004
			PLICANT	First Named Inventor	Roger D. Tung et al.
	OTATEMENT BY ATTERANT			Art Unit_	1625
(use	(use as many sheets as necessary)			Examiner Name	D. Margaret Seaman
Sheet	4	of	5	Attorney Docket Number	VPI/92-07CIP2ADIV3 CON

		NON PATENT LITERATURE DOCUMENTS	-
Examiner initials*	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T²
		G.D. Hartman et al., "4-Substituted Thiophene- and Furan-2-sulfonamides as Topical Carbonic Anhydrase Inhibitors", <u>J. Med. Chem.</u> , 35, pp. 3822-31 (1992).	
		J.R. Huff, "HIV Protease: A Novel Chemotherapeutic Target for AIDS", <u>Journal of Medicinal Chemistry</u> , 34(8), pp. 2305-14 (1991).	
		K.Y. Hui et al., "A Rational Approach in the Search for Potent Inhibitors Against HIV Proteinase", FASEB, 5, pp. 2606-10 (1991).	
		N.E. Kohl et al., "Active HIV Protease Is Required for Viral Infectivity", Proc. Natl. Acad. Sci. USA, 85, pp. 4686-90 (1988).	
		X. Lin et al., "Enzymic Activities of Two-Chain Pepsinogen, Two-Chain Pepsin, and the Amino-Terminal Lobe of Pepsinogen", <u>J. Biol. Chem.</u> , 267(24), pp. 17257-63 (1992).	
		K.P. Manfredi et al., "Examination of HIV-1 Protease Secondary Structure Specificity Using Conformationally Constrained Inhibitors", J. Med. Chem., 34, pp. 3395-99 (1991).	
		F.R. Marshall, "Computer-Aided Drug Design", Ann. Ref. Pharmacol. Toxicol., 27. pp. 193-213 (1987).	
-		J.A. Martin, "Recent Advances in the Design of HIV Proteinase Inhibitors", Antiviral Research, 17, pp. 265-78 (1992).	
		T.D. Meek et al., "Inhibition of HIV-1 Protease in Infected T-Lymphocytes by Synthetic Peptide Analogues", Nature, 343, pp. 90-92 (1990).	
		M. Miller et al., "Structure of Complex of Synthetic HIV-1 Protease with a Substrate-Based Inhibitor at 2.3 Å Resolution", Science, 246, pp. 1149-52 (1989).	
		M. Miller et al., "Crystal Structure of a Retroviral Protease Proves Relationship to Aspartic Protease Family", Nature, 337, pp. 576-79 (1989).	
		H. Mitsuya and S. Broder, "Inhibition of the in vitro Infectivity and Cytopathic Effect of Human T-Lymphotropic Virus Type III/Lymphoadenopathy-Associated Virus (HTLV-III/LAV) by 2',3'-Dideoxynucleosides", Proc. Natl. Acad. Sci. USA, 83, pp. 1911-15 (1986).	
		K.H.M. Murthy et al., "Crystal Structures at 2.2-Å Resolution of Hydroxyethylene-Based Inhibitors Bound to Human Immunodeficiency Virus Type 1 Protease Show That the Inhibitors Are Present in Two Distinct Orientations", <u>J. Biol. Chem.</u> , 267, pp.22770-78 (1992).	
		J.B. Nichols et al., "A Molecular Mechanics Valence Force Field for Sulfonamides Derived by ab initio Methods", J. Phys. Chem., 95, pp. 9803-11 (1991).	
		L.E. Overman and L.A. Flippin, "Facile Aminolysis of Epoxides with Diethylaluminum Amides", <u>Tetrahedron Letters</u> , 195, pp. 195-98 (1981).	
		J. Palca, "Shooting at a New HIV Target", Science, 247, p. 410 (1990).	
		L.H. Pearl et al., "A Structural Model for the Retroviral Proteases", Nature, 329. pp. 329-51 (1987).	

Examiner	Date
Signature	Considered

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO			то	Complete if known	
1				Application Number	10/786,997
INFO	DRMATION	DISC	CLOSURE	Filing Date	February 24, 2004
STATEMENT BY APPLICANT			PLICANT	First Named Inventor	Roger D. Tung et al.
•				Art Unit	1625
(use	(use as many sheets as necessary)			Examiner Name	D. Margaret Seaman
Sheet	5	of	5	Attorney Docket Number	VPI/92-07CIP2ADIV3 CON

		NON PATENT LITERATURE DOCUMENTS	
Examiner initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
		M. Popvic et al., "Detection, Isolation, and Continuous Production of Cytopathic Retroviruses (HTLV-III) from Patients with AIDS and Pre-AIDS", <u>Science</u> , 224, pp. 497-500 (1984).	
		G.H. Posner and D.Z. Rogers, "Organic Reactions at Alumina Surfaces. Mild and Selective Opening of Epoxides by Alcohols, Thiols, Benzeneselenol, Amines, and Acetic Acid", <u>J. Am. Chem. Soc.</u> , 99, 8208-18 (1977).	
		M.D. Power et al., "Nucleotide Sequence of SRV-1, a Type D Simian Acquired Immune Deficiency Syndrome Retrovirus" Science , 231, pp. 1567-73 (1986).	
		N.A. Roberts, "Rational Design of Peptide-Based HIV Proteinase Inhibitors", <u>Science</u> , 248, pp. 358-61 (1990).	
		S. Scharpe et al., "Proteases and Their Inhibitors: Today and Tomorrow", <u>Biochimie</u> , 73, pp. 121-26 (1991).	
		S.K. Sharma et al., "Could Angiotensin I Be Produced from a Renin Substrate by the HIV-1 Protease?", Anal. Biochem., 198, pp. 363-67 (1991).	
		H. Toh et al., "Close Structural Resemblance Between Putative Polymerase of a Drosophila Transposable Genetic Element 17.6 and pol Gene Product of Moloney Murine Leukemia Virus", EMBO J., 4. pp. 1267-72 (1985).	
		,	

Examiner	Date	
Signature	Considered	

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered.

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation in not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-4450. Alexandria, VA 22313-1450.